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Progressive multifocal leukoencephalopathy as the first manifestation of sarcoidosis : a case report. S. De Raedt, M.D., A. Michotte, M.D., P. Lacor, M.D., A. Flamez, M.D., G. Ebinger, Ph.D., M.D. (Departments of neurology and infectiology AZ VUB).

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease caused by a polyomayirus, called JC-virus. PML occurs mainly in immunocompromised hosts. We report a case of PML as a first manifestation of sarcoidosis in a 43 year-old previously healthy man. Patient presented with speech disturbances, followed by weakness of the left arm and the left leg. Brain, MRI disclosed a diffuse hyperintense lesion of the white matter in the right parietal and occipital lobes on T2 weighted images. A brain biopsy revealed severe white matter destruction, an increased number of macrophages, a lot of bizarre shaped astrocytes and enlarged oligodendrocyte nuclei containing viral inclusions, all together pathognomonic for a very active form of PML. T-lymphocytopenia, an elevated angiotensin converting enzyme, non caseating bone marrow granulomas and a high CD4/CD8 ratio in bronchoalveolar lavage, leaded to the diagnosis of sarcoidosis, with as most important manifestation a cellular immunodeficiency (T-lymphocytopenia,) causing PML. After starting a treatment with cidofovir, one of the very few drugs that have shown to be useful in treating PML, we remarked a neurological and radiological stabilization. To our knowledge the association of PML, and sarcoidosis without previous immunosuppressive treatment is described in only a few cases, none of them were treated with cidofovir.

Chronic inflammatory demyelinating polyneuropathy in a diabetic patient : favorable response to corticosteroids after failure of intravenous immunoglobulins treatment. K. Pedersen, M. Pandolfo, N. Mavroudakis (Department of Neurology, Hôpital Erasme, Université Libre De Brussels, Route De Lennik 808, 1070 Brussels, Belgium).

Chronic Inflammatory Demyelinatirig Polyneuropathy (CIDP) is an immunomediated inflammatory disorder of the peripheral nervous system. The pathological hallmarks of CIDP are segmental demyelination and remyelination and inflammatory infiltrates. Several diagnostic criteria have been proposed : AAN, INCAT, Nicolas, Thaisetthawatkul.

We report the case of a 54-year old type-2 diabetic female patient who progressively developed distal hypoesthesia and weakness of the four limbs. Diabetes control was good. A diagnosis of CIDP was evoked in an other hospital and she was treated twice by Intravenous immunoglobulin (IVIG). After the first course, a transient favourable response was observed during 3 days. The patient became thereafter rapidly wheelchairbound despite the second course of IVIG. On admission in our institution, other diagnosis were excluded. The patient met AAN clinical and electrophysiological criteria for the diagnosis of CIDP. A treatment with corticosteroids was initiated : one month later, the patient was able to walk alone.

CIDP may be isolated or associated with systemic diseases. Several studies indicate that CIDP patients with diabetes (DM-CIDP) and patients with idiopathic CIDP have similar features and responses to treatment.

CIDP recognised treatments include plasma exchange, corticosteroids and IVIG. All treatments efficacy seems to be equivalent. There is a trend to consider IVIG as first line treatment for DM-CIDP patients.

We report the case of a type 2 diabetic patient, whose condition rapidly deteriorates after IVIG treatment. In contrast clinical response to corticosteroids was spectacular. This case raises the question of the choice of the immunomodulatory treatments, particularly in diabetic patients.

Antigen-driven immunoblots and polymerase chain reaction in cerebrospinal fluids from 35 patients with suspected varicella-zoster infection of the nervous system. S. Grégoire, C. J. M. Sindic (Service de Neurologie, Université catholique de Louvain, Cliniques Universitaires Saint Luc, Brussels, Belgium).

Objective : Cerebrospinal fluid (CSF) analysis is a key tool in the diagnosis of central nervous system (CNS) infection with varicella-zoster virus (VZV). The detection of an intrathecal synthesis of VZV-specific antibodies and the amplification of VZV DNA by polymerase chain reaction (PCR) are well-established techniques. We present a detailed CSF analysis of patients suspected to harbor CNS VZV infection and we discuss correlations between CSF analysis and clinical pictures.

Materials & methods : Thirty-five patients were included and distinguished in three groups. The first one consisted of 28 cases (80%) with a rash in one or more dermatomes and clinical suspicion of radiculitis or meningitis. These patients were divided in three subgroups according to the affected dermatomas : trigeminal (N = 9 ; 32%), facial (N = 11 ; 40% and cervico-thoraco-lumbar (N = 8 ; 28%). The second group consisted of four patients (11%) presenting radiculitis (N = 2) or meningo-encephalitis (N = 2) signs without eruption (zoster “sine herpete”). The third group contained three patients (9%), with generalized rash and encephalitis. A PCR for VZV DNA in the CSF and antigen-driven immunoblots were performed in all cases.

Results : Among the 28 cases with radiculitis, CSF pleocytosis was observed in 86%. PCR was positive in 22% within the trigeminal group, whereas it was positive in 64% and in 50% within the facial and cervico-thoraco-lumbar subgroups, respectively. In addition, an intrathecal synthesis of oligoclonal antibodies with anti-VZV activity was detected in 39% of this first group. The CSF collected from both patients with zoster “sine herpete” and radiculitis displayed pleiocytosis. A positive VZV PCR and an intrathecal synthesis of VZV specific antibodies were detected in one patient each. Both patients with meningoencephalitis without eruption had positive PCR and CSF analysis also detected oligoclonal anti-VZV antibodies in one. Finally, CSF PCR was positive in two of the three patients with generalized rash and encephalitis. One of them had associated pleocytosis. This patient underwent a second lumbar puncture which revealed a negative PCR and a local production of VZV antibodies. The last patient of this group displayed an intrathecal synthesis of VZV antibodies while PCR was not done.

Conclusion : Our findings highlight the diagnostic value of a detailed CSF analysis in VZV infection. This is particularly true in facial palsy and intercostal zona with suspected meningitis because of frequent CSF abnormalities. VZV may be a causative agent in cases with meningitis or radiculitis of unknown origin, even in the absence of skin manifestations. In such patients rapid diagnosis by PCR amplification of VZV DNA and detection of intrathecal antiVZV antibodies allow early antiviral therapy.

Smoking preceding Parkinson’s disease. J. De Reuck[1],*, M. De Weweire[1], G. Van Maele[2], P. Santens[1] ([1]Department of Neurology and [2]Department of Medical Statistics, University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium).

Background : There is growing evidence from case-control and from cohort studies that smoking is inversely related to the risk of developing Parkinson’s disease (PD). However, it is still controversial if PD starts at an older age in ever-smoking patients compared to never-smoking ones.

Patients and methods : The present retrospective study compares in a large series of 512 out-patients, collected over the last 24 years, the age of onset of the complaints, the age at which PD was diagnosed and the start of levodopa treatment between ever- and never-smokers. Also the occurrence of longterm side-effects of the drug was evaluated. 184 PD patients with a history of smoking were compared with 328 who had never smoked. The subgroups with and without a family history of PD were analysed separately.

Results : In the overall ever-smoking group, as well as in the subgroup without a family history, the onset of the disease and the time of the diagnosis of PD and the time at which levodopa was started occurred at an older age than in the never-smoking group. This difference could not be demonstrated in the patients with a family history, due to the low number of cases and the lack of statistical power. Although the follow-up period was the same in both study groups, motor fluctuations and dyskinesia were more frequent and appeared earlier after levodopa treatment in the non-smoking compared to the ever-smoking PD patients. Only for cognitive impairment there was a non-significant increased trend in the smoking group.

Conclusion : The present study confirms the protective action of smoking on PD and also suggests some modulating effect of smoking on the dopaminergic system.

Influence of pre-stroke dementia on the risk of post-stroke epileptic seizures. Ch. Cordonnier, M.D., H. Hénon, M.D., Ph.D., Ph. Derambure, M.D., Ph.D., F. Pasquier, M.D., Ph.D., D. Leys, M.D., Ph.D. (From *EA 2691*. Department of Neurology. Stroke Unit (Drs. Cordonnier, Hénon, Leys), Memory Clinic (Dr. Pasquier), and Neurophysiology department (Dr Derambure), University of Lille, Lille, France).

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Background : Seizures occur in 10% of stroke patients but predictive factors are not clearly identified. Patients with dementia have an increased risk of seizures compared to a general population. In a population of patients admitted for a stroke, 16% have a preexisting dementia and the cumulative proportion of demented patients is of 28,5% after a follow-up of 3 years. However, relationship between dementia and seizures remains unclear.

Objective : To evaluate whether patients with preexisting dementia have an increased risk of seizures after a stroke.

Methods : The study was conducted in the 202 consecutive stroke patients recruited in the Lille Stroke/Dementia study (97 men ; median age : 75 ; range : 42-100). We evaluated pre-stroke cognitive functions using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), with a cut-off of 104 for the diagnosis of dementia. Seizures were defined as early (ES) when occurring within 7 days after the stroke and as late (LS) when occurring more than 7 days after the stroke. We analysed the relationship between seizures and pre-stroke dementia with the Chi-square test for ES, and Kaplan-Meier analysis for LS.

Results : 33 (16.3%) patients were identified as demented before stroke. Among the 202 patients, 11 (5.4%) developed an ES and 14 (6.9%) developed LS. Preexisting dementia was not associated with the occurrence of ES but was independently associated with the occurrence of LS (RR = 4.66 ; 95% : 1.34-16.21).

Conclusion : Our study, which is the first to address this issue, showed that patients with preexisting dementia have an increased risk of late post-stroke epileptic seizures.

Influence of epileptic seizures on the cognitive outcome in a cohort of stroke patients. Ch. CORDONNIER, M.D., H. HÉNON, M.D., Ph.D., Ph. DERAMBURE, M.D., Ph.D., F. PASQUIER, M.D., Ph.D., D. LEYS, M.D., Ph.D. (From *EA 2691*. Department of Neurology, stroke department (Drs. Cordonnier, Hénon, Leys), memory clinic (Dr. Pasquier), and clinical neurophysiology clinic (Dr Derambure). University of Lille, Lille, France.
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Background : Seizures occur in 10% of stroke patients. Several studies have shown that early seizures (ES) were associated with a higher in-hospital mortality. Data regarding the influence of seizures on the functional outcome are scarce and controversial. No study has addressed the issue of the influence of seizures on the cognitive outcome in a cohort of stroke patients.

Objective : To evaluate the influence of ES on the risk of dementia within 3 years after stroke.

Methods : The study was conducted in the 202 consecutive stroke patients recruited in the Lille Stroke/Dementia study (97 men ; median age : 75 ; range : 42-100). Seizures were defined as early when occurring within 7 days after stroke. During the follow-up, dementia was diagnosed according to the ICD-10 criteria. We analysed the relationship between ES and the risk of in-hospital mortality with logistic regression and Kaplan-Meier analyses. We evaluated the relationship between ES and new-onset dementia after stroke, with a Kaplan-Meier analysis and a Cox model, after exclusion of patients with pre-existing dementia (defined as a score of 104 or more at the Informant Questionnaire on Cognitive Decline in the Elderly [IQCODE]).

Results : 33 (16.3%) patients were identified as demented before stroke. Among the 202 patients., 11 (5.4%) developed an ES : ES were associated with a higher in-hospital mortality rate (RR = 9.28 ; 95% CI : 1.65-52.20) and a higher risk of new-onset dementia within 3 years (RR = 3.81 ; 95% CI : 1.13-12.82).

Conclusion : In a cohort of stroke patients, ES are associated with an increased risk of new-onset dementia within 3 years after stroke onset.

Reorganisation of the cortical motor areas in congenital hemiplegia. fMRI and TMS studies. Y. VANDERMEEREN[1], A. DE VOLDER[2,3], M. DAVARE[1], C. GRANDIN[4], G. COSNARD[4], J.-L. THONNARD[5], G. SÉBIRE[6], E. OLIVIER ([1]Laboratory of Neurophysiology ; [2]Lab. Génie Réhab. Neurale, [3]Pediatric Neurology Service, St. Luc Hospital ; [4]Neuroradiology department, fMRI section, St. Luc Hospital ; [5]Laboratory of Physical Medicine and Rehabilitation, Faculty, of Medecine, Université eatholique de Louvain (UCL), Brussels, Belgium ; [6]Child Neurology Department, Université de Sherbrooke. Canada).

Whereas a unilateral injury of the primary motor cortex (M1) or corticospinal tract during the perinatal period often results in severe congenital hemiplegia (CH), it could also be followed by an impressive recovery. Functional magnetic resonance imaging (fMRI) consistently disclosed widespread bilateral activation during paretic hand movements, suggesting that the reorganisation processes which underlie functional recovery may involve the damaged and intact hemispheres.

First, in order to unveil which cortical areas underlie recovery in CH, SPM99 was used to disclose a positive correlation between the fMRI activation intensity, and fniger dexterity. fMRI was performed during sequential paretic and non-paretic fingers movements in 6 children with CH of cortical origin and 6 age-matched controls. In the intact hemisphere of CH patients, the fMRI activation in the lateral premotor and posterior parietal cortices correlated positively with paretic hand's residual dexterity, suggesting that the intact hemisphere was adaptively involved in the control of paretic hand.

Secondly, since every non-primary motor area sends corticomotoneuronal (CM) projections to both sides of the spinal cord (Dum & Strick, 2002), the adaptive recruitment of CM projections originating outside M1 could underlie recovery. Thus, in 12 CH patients and 12 controls, the representation of both hands (mapped by transcranial magnetic stimulation) was co-registered with 3D-MRI. For the paretic hand, both crossed and uncrossed CM projections originated exclusively from the M1hand representation, as observed for non-paretic hand and in controls.

In conclusion, whereas adaptive recruitment of non-primary motor areas in CH patients likely underlies recovery, the fMRI over-activation found in the intact cortex outside the M1 hand representation does not reflect the recruitment of "alternative" CM projections since both crossed and uncrossed CM neurones related to the paretic hand are confined exclusively to the MI hand representation.

Reference

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Analgesic potentials of vagal nerve stimulation : review of the literature and experimental data. C. LEGRAIN, S. MULTON, M. SCHOLSEM, D. MARTIN, J. SCHOENEN (Center for Cellular & Molecular Neurobiology, Neuroanatomy laboratory, University of Liège).

The first investigations on the modulation of nociception by vagal afferents were performed approximatively 20 years ago and a large body of experimental data now exists suggesting that vagus nerve stimulation (VNS) is of potential interest in pain treatment. The analgesic effect of VNS seems to depend on a critical stimulation intensity that activates C fibres. Studies in animals show that low intensity stimulations of cervical vagal afferents facilitate, whereas high intensity stimulations inhibit nociceptive responses or noxious heat-induced Fos expression. However, the latter experiments have applied VNS with a stringent duty cycles, which may hardly be tolerable in patients.

We undertook therefore a study of VNS in rats with the devices and stimulator used in epilepsy treatment in order to assess the effects on various pain models of different stimulation protocols and to investigate the mechanisms by which VNS may modulate pain.

We studied in rats the effect on trigeminal nociception of left cervical VNS applied for 3 days with 1.5 mA intensity, 20 Hz frequency, 1 ms pulse width and a duty cycle of 30 s ON/ 5 min OFF, using an implantable electrode and the NCP-Cyberonics® pulse generator. Injection of formalin (50µl, 5%) into the left mystacial vibrissae was used as a classical model of orofacial inflammatory pain. Nociceptive behaviour, i.e. rubbing of the injected site, was quantified until 50 min post-injection and compared between 3 groups of animals : a VNS group that received vagal stimulation, a SHAM group implanted but not stimulated and a FOR non-implanted group. In addition to nociceptive behaviour, mechanical allodynia was compared with von Frey hairs in the three groups 4 hours after the formalin injection. Thereafter, animals were sacrificed and the brain, brain stem and upper cervical cord prepared for immunohistochemical analysis.

Behavioural results show that VNS significantly reduces typical responses to facial pain by comparison with both conditions without stimulation (SHAM and FOR). The nociceptive behaviour is decreased on average by 50%. Furthermore, the formalin injection induces a significant mechanical allodynia in the FOR group, but not in the VNS group.

On FOS-immunohistochemistry, labelled nuclei (a marker of neuronal activity) in trigeminal nucleus caudalis (TNC) laminae I-II are significantly more numerous on the formalin injection side. Unlike in our previous study of a more stringent VNS duty cycle (20s ON/18 s OFF), the formalin-induced increase of Fos expression is not attenuated in VNS-treated animals suggesting that the mechanisms of VNS-induced antinociception might vary with the stimulation parameters. The lack of significant FOS reduction could be due to a supraspinal rather than a spinal effect of VNS with the protocol used in epilepsy or to a more pronounced activation of local (e.g. GABAergic) interneurons which would compensate a decrease of FOS-positive secondary nociceptors. The immunohistological expression of neuronal NO-synthase (nNOS) in TNC, however, is decreased by VNS which suggests that a spinal/medullary effect is also present. The decrease in nNOS expression could explain the reduction by VNS of formalin-induced pain and allodynia.

Taken together, our results suggest that VNS, applied with devices and a stimulation protocol used in human epilepsy therapy has promising antinociceptive effects in a rat model of trigeminal inflammatory pain.
